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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/521,264	03/08/00	GROMAN	E 1275/190
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EXAMINER

WELLS, L

ART UNIT

PAPER NUMBER

1619

DATE MAILED:

11/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/521,264

Applicant(s)

GROMAN ET AL.

Examiner

Lauren Q Wells

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 October 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13,18-29,35,36 and 39-66 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13,18-29,35,36 and 39-66 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. 6) ☐ Other: _____

DETAILED ACTION

Claims 1-13, 18-29, 35-36, and 39-66 are pending. Claims 14-17, 30-34, and 34-38 were cancelled per the Amendment received October 9, 2001, Paper No. 6. Claims 57-66 were added per the Amendment received October 9, 2001, Paper No. 6.

Response to Applicant's Arguments/Amendment

The Applicant's arguments filed October 9, 2001 (Paper No. 6) to the rejection of claims 1-66 made by the Examiner under 35 USC 103, and 112 and to the objection to the specification have been fully considered and deemed not persuasive. The Applicant's arguments to the rejection of claims 14, 16, 17, 30, 35-38 made by the Examiner under 35 USC 102 have been fully considered and deemed persuasive per the Applicant's cancellation and amendment to the claims.

Specification Objection Maintained

The objection to new matter on page 1 (lines 25-26), page 17 (lines 20-21), page 19 (lines 22-23) and page 45 (line 22) is maintained. Again, Applicant is required to cancel the new matter in the reply to this Office Action. In the event that the new matter is not cancelled, the Examiner respectfully asks Applicant to point out support for the new matter with page and line numbers in the specification.

The Examiner respectfully notes that the Applicant did not respond to this objection in the Amendment received October 9, 2001, Paper No. 6.

112 Rejection Maintained

The rejection of claims 5, 10-12, 14-15, 21-22, 26-30, 35-37, 53-54 and newly added claims 57, 59, and 64-66 under 35 U.S.C. 112 is MAINTAINED for the reasons set forth in the Office Action mailed October 9, 2001, Paper No. 6, and those found below.

(i) The term “derivitized” is vague and indefinite, as this phrase encompasses a vast number of chemical compounds and polymers when used in conjunction with the phrase polysaccharide. It is not possible for one of ordinary skill in the art to be apprised of all these chemical compounds.

(ii) The terms “enhanced” and “ultrasmall” are relative. These terms encompass broad size ranges and benefits/increases. Thus, one of ordinary skill in the art would not be apprised of all the size ranges and benefit/increases encompassed by this phrase.

(iii) Claims 35 and 36 are vague and indefinite. What is being claimed, a method of administration or a method of decreasing edema?

(iv) Claims 57 and 59 are vague and indefinite. The phrase “of the type for deriving a composition for pharmacological use from a polysaccharide” is confusing. Does this mean that other methods other than that stated in claim 57 are being claimed? What is deriving a composition for pharmacological use from a polysaccharide? What method is being claimed, a method of making a composition or a method of decreasing edema? What is “providing an extent of carboxylation sufficient to produce a decreased edematous response”? This phrase is relative.

103 Rejection Maintained

The rejection of claims 1-13, 18-29, 35-36, 39-56 and newly added claims 47-66 under 35 U.S.C. 103(a) as being unpatentable over Maruno et al. (5,204,457) or Maruno et al. (6,165,378) in view of Josephson et al. (5,160,726) or Lewis (5,055,288) or Groman et al. (4,827,945) in further view of Golamn et al. (5,985,245) is MAINTAINED for the reasons set forth in the Office Action mailed July 5, 2001, Paper No. 5, and those found below.

Applicant argues "The Maruno et al. patents show only heating to 80 C, and teach away from autoclaving", "Maruno '487 teaches that autoclaving causes breakdown of the composition" and that "Josephson et al. shows that there is increased toxicity associated with autoclaving polysaccharide-based MRI agents". This argument is not persuasive. Josephson teaches that the preference for terminal sterilization, which comprises autoclaving, over filter sterilization on the basis of sterility assurance, the generally low acute toxicity observed with terminally sterilized iron oxide preparations, and the difficulty of visually detecting microbial contamination, all combine to suggest that terminal sterilization is the method of choice for parenteral superparamagnetic iron oxide colloids. Maruno and Maruno both teach filter sterilization of superparamagnetic iron oxide colloids. Hence, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have substituted the terminal sterilization of Josephson for the filter sterilization of Maruno and Maruno.

Applicant argues, "while Lewis et al. shows autoclaving, it is only after citrate is added. However there is not reduce polysaccharide". This is not persuasive. Lewis teaches sterilizing superparamagnetic iron oxides by autoclaving. Furthermore, Lewis teaches that while autoclaving is the preferred technique for sterilization since the bottle or container need not be sterile prior to fill, an alternative to sterilization is filtration, but that superparamagnetic fluids at

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high concentrations filter poorly. Hence, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have substituted the sterilization step of autoclaving of Lewis for the filter sterilization of Maruno and Maruno.

Applicant argues, "there are no reduced or carboxyalkylated polysaccharides in Groman et al. therefore Groman et al. teaches nothing about such materials". This argument is not persuasive. Groman teaches sterilizing superparamagnetic iron oxides by autoclaving. Furthermore, Groman teaches that concentrated solutions of aqueous superparamagnetic materials cannot be sterilized by filtration even when the solution is comprised of materials smaller than the pore of the filter because filter-sterilized, dilute material can be reconcentrated and dispensed into sterile bottles, offering many chances to recontaminate the product, but autoclaving solutions of superparamagnetic materials after bottling is preferable, since sterilization is achieved after final bottling, and there is little opportunity for contamination of the final product. Hence, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have substituted the sterilization step of autoclaving of Groman for the filter sterilization of Maruno and Maruno.

Applicant argues, "Golman et al. . .all of these materials are in fact metal chelation complexes. . .while dextrans are part of this complex, they are neither reduced, nor carboxyalkylated, and certainly not both". This argument is not persuasive, as this reference was not relied upon for its teachings of reduced dextrans, but for its teachings of kits comprising superparamagnetic species.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on

combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion


THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is (703) 305-1878. The examiner can normally be reached on M-F (7-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Diana L Dudash can be reached on (703) 308-2328. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.


DAMERON L. JONES
PRIMARY EXAMINER

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lqw

October 23, 2001